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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/306,780	05/07/99	TAKEMURA	F	2084-0046-0D

022850 HM12/1118
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EXAMINER	
HINES, J	

ART UNIT	PAPER NUMBER
1641	6

DATE MAILED: 11/18/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/306,780	Applicant(s) Takamura et al.
	Examiner Ja-Na Hines	Group Art Unit 1641

☒ Responsive to communication(s) filed on *Sep 7, 1999* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-32* is/are pending in the application.

Of the above, claim(s) *1-16* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *17-32* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Amendment Entry

1 The amendment filed September 7, 1999 has been entered. Claims 1-16 have been canceled. Claims 17-32 are pending.

Priority

2. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Specification

3. The disclosure is objected to because of the following informalities: The acronym HCV and BSA are not defined within the specification. Appropriate correction is required.

4. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Sequence Compliance

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) that the sequence in the instant application should refer to a sequence in the following way "SEQ ID NO 2".

APPLICANT IS GIVEN A THE TIME SET FORTH IN THIS OFFICE ACTION WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Claim Objections

6. Claims 23 and 24 are objected to because of the following informalities: they should refer to sequence no 2 in the following way, "SEQ ID NO 2." Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 17-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takahara et al., in view of Weiner et al. Takahara et al., teaches a biologically active polypeptide linked to a substance containing an amino acid donor having the ability to bind a nucleic acid (abstract). Takahara et al., also teaches a large number of biologically active polypeptides including peptides derived from microorganisms and viral genes (page 2 lines 6-13 and lines 30-32). Many biologically active peptides bind specifically to corresponding receptors in cells, while antibodies bind to their antigens and these polypeptides can be used as targeting molecules which utilize their specific binding ability (page 2 lines 13-19). It is known to link proteins and polypeptides to each other using a recombinant DNA method in which genes are combined with each other and the process has several advantages, including the ability to link substances which produce fusion proteins and they can be bound to the N-terminal or C-terminal of another

protein, thus the active center is present in the terminal of the protein (pages 3- 4 lines 52-5). However, Takahara et al., does not teach the use of the nucleic acid bound polypeptide assayed in an immunoassays.

Weiner et al., teaches immunoreactive polypeptides wherein the polypeptides comprises an amino acid sequence from the hepatitis C virus. Weiner et al., teaches a method of detecting antibodies by providing a sample containing antibodies; reacting the sample with the immunoreactive polypeptides, which are antigens; allowing the formation of antigen-antibody complexes; and detecting the formation (col. 3 lines 5-16). The polynucleotides are the polymeric form of nucleotides of any length, either ribonucleotides or deoxyribonucleotides (col. 7 lines 38-40). For diagnostic application the polypeptides can be used directly in a homogeneous or heterogeneous immunoassay format, where the polynucleotide in immobilized on a solid substrate such as a plastic bead (col. 14 lines 36-44). The "..design of the immunoassay is subject to a great deal of variation, and variety of these are known in the art. However, the immunoassay will use antigen sets wherein each antigen set consists of a plurality of substantially identical polypeptides comprising the amino acid sequence..." (col. 21 lines 52-58). Protocols for immunoassays may be use solid supports or be by immunoprecipitation (col. 21 lines 62-63). Most assays involve the use of labels which may be fluorescent, chemiluminescent, radioactive, or dye molecules, some assays will utilize biotin and avidin, while other assays will be enzyme labeled and mediated immunoassays, like ELISA (col. 21-22 lines 63-3).

Therefore, it would have been obvious at the time of applicant's invention to have used the biologically active polypeptide linked to an amino acid donor having the ability to bind a nucleic acid as taught by Takahara et al., with the immunoassay as taught by Weiner et al., because Weiner et al., teaches polypeptides expressed in the form of a fusion polypeptide by genetic engineering, wherein the polypeptide is an antigen can be assayed in an immunoassay.

8. Claims 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takahara et al., in view of Weiner et al., in further view of Ono et al. Takahara et al., and Weiner et al., have been discussed above, however neither does teach SEQ ID NO 2. Ono et al., teaches the complete nucleotide sequence of the cloned hepatitis B virus. These sequences have 100% sequence identity the instant application's amino acid sequence. Ono et al., teaches the complete nucleotide sequence of different subtypes of hepatitis B virus (HBV) cloned in *E. coli* and discuss the differences in the nucleotide sequences among different subtypes (page 1747). Ono et al., also teaches that analysis of viral mRNA is necessary for a more precise understanding of the genetic organization (page 1756).

Therefore, it would have been obvious at the time of applicant invention to have used the Ono et al., hepatitis virus sequence, in the immunoassay of Takahara et al., and Weiner et al., because Ono et al., teaches the complete nucleotide sequence which is important in the understanding of the genetic system.

9. Claims 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takahara et al., in view of Gibbons. Takahara et al., has been discussed above, however Takahara et al., does not teach agglutination assays. Gibbons teaches a method of detecting the presence or amount of agglutination of particles in a reaction medium (col. 2 lines 15-24). The method steps comprise forming a reaction medium containing (1) a sample; (2) a plurality of particles having a binding pair member bound to their surfaces; and (3) a monovalent complementary partner to said binding pair member to which is attached an analyte mimic or analyte binding partner; and detecting the presence of agglutination of said particles in the reaction medium (col. 2 lines 15-24). Examples of such binding pairs include antigens and antibodies and complementary nucleic acid strands (col. 5 lines 38-42). Agglutination assays do not require expensive detection equipment, can be visually read agglutination, usually qualitative and can be readily adaptable to instrumental quantitation (col.1 lines 28-61).

Accordingly, it would have been obvious to use the agglutination assay of Gibbons with the antigen comprising a nucleic acid bound polypeptide as taught by Takahara et al., because Gibbons teaches binding pairs include antigens and antibodies or complementary nucleic acid strands; that agglutination assays do not require expensive detection equipment; and can be readily adaptable to instrumental quantitation.

10. Claims 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Takahara et al., in view of Gibbons, in further view of Ono et al. Takahara et al., and Gibbons, have been discussed above, however neither does teach SEQ ID NO 2. Ono et al., teaches a sequences which has 100% sequence identity the instant application's amino acid sequence. Ono et al., teaches the complete nucleotide sequence of different subtypes of hepatitis B virus (HBV) cloned in *E. coli.*

Therefore, it would have been obvious at the time of applicant invention to have used the Ono et al., hepatitis virus sequence, in the immunoassay of Takahara et al., and Gibbons, because Ono et al., teaches the complete nucleotide sequence which is important in the understanding of the genetic system.

Prior Art

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Valenzula et al., teaches immunogenic compositions involving viral particles composed at least in part of hybrid proteins of at least a portion of a particle forming protein and one or more polypeptides having at least one epitope of interest. Nucleic acid sequences are employed for coding and expression of the hybrid protein and can be used for diagnostic purposes (abstract). Liebermann et al., teaches the nucleic acid binding proteins possessing a recognition motif sufficient to cause binding of the protein to the DNA or RNA using recombinant technology. Birnbaum et al., teaches the use and presence of the hepatitis B virus core protein nucleic acid binding motif and stability which can lead to use in fusion proteins. Okamoto et al., Pasek et al., Fujiyama et al., Kobayashi et al., and Gailbert et al., all

teaches the nucleotide sequence of the hepatitis B virus genome with at least 97.3% sequence identity to SEQ ID NO 2 of the instant application.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines

November 16, 1999

James C. Housel 11/17/99

JAMES C. HOUSEL
SUPERVISORY PATENT EXAMINER